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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/508,319	07/17/2012	Christopher Y. Park	STAN-696	1703

77974 7590 02/23/2017

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ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
02/23/2017	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CHRISTOPHER Y. PARK, WENDY W. PANG, and IRVING L. WEISSMAN[1]

Appeal 2015-007714
Application 13/508,319
Technology Center 1600

Before TAWEN CHANG, TIMOTHY G. MAJORS, and DAVID COTTA, *Administrative Patent Judges*.

CHANG, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of phenotyping a myelodysplastic condition,[2] which have been rejected as lacking in patentable subject matter. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] Appellants identify the Real Party in Interest as the Board of Trustees of the Leland Stanford Junior University. (Br. 1.)

[2] A myelodysplastic condition is a type of hematologic (i.e., blood) disorder. (Spec. ¶ 1.)

STATEMENT OF THE CASE

Myelodysplastic syndromes (MDS) represent a related group of clonal hematologic disorders characterized by reduced number of peripheral blood cells due to ineffective blood cell production. (Spec. ¶ 1.) The Specification states that "diagnosis [of MDS] remains a clinical challenge due to the absence of a single objective criterion for diagnosis, except in the cases where conventional cytogenetics may reveal a clonal abnormality." (*Id.* at ¶ 4.) According to the Specification,

> [i]n the methods of the invention, hematologic samples . . . are differentially analyzed for the distribution of hematopoietic stem and progenitor cells among specific phenotypes [including] hematopoietic stem cells (HSC); myeloid progenitors; common lymphoid progenitors (CLP); megakaryocyte progenitors; *etc*. Specifically, it is shown that myelodysplastic syndromes . . . show reproducible alterations in hematopoietic stem cell and myeloid progenitor cell frequency, with decreased . . . granulocyte/macrophage progenitors (GMP) and increased . . . hematopoietic stem cells.

(*Id.* at ¶ 6.) Further according to the Specification, "[a]n analysis based on the presence of cell surface markers that provide an assignment of cells into a class of interest, are generally used for determining the distribution of phenotypes in a patient sample." (*Id.* at ¶ 7.)

Claims 1, 6, and 7 are on appeal. Claim 1 is illustrative and reproduced below:

> 1. A method of phenotyping a myelodysplastic condition, the method comprising:
>
> combining a hematologic sample from a patient suspected of said myelodysplastic condition with antibodies specific for CD34, CD38 and CD45RA;
>
> determining the distribution of progenitor cells between hematopoietic stem and progenitor subsets as follows:

> $CD34^+CD38^-$ hematopoietic stem cells (HSC), $CD34^+CD38^+CD45RA^-$ common myeloid progenitor (CMP), $CD34^+CD38^+CD45RA^-$ megakaryocyte erythroid progenitors (MEP) and $CD34^+CD38^+CD45RA^+$ granulocyte/macrophage progenitors (GMP)
>
> wherein an increase in the fraction of HSC and a decrease in the fraction of myeloid progenitor cells that are granulocyte macrophage progenitor cells relative to a normal control of at least 1.5 fold is indicative of an initial diagnosis of myelodysplastic syndrome (MDS).

(Br. 9 (Claims App'x).)

The Examiner rejects claims 1, 6, and 7 under 35 U.S.C. § 101 as being lacking in patentable subject matter. (Ans. 2.)

DISCUSSION

Issue

The Examiner finds that claims 1, 6, and 7 are directed to a law of nature, i.e., "[t]he relationship between hematopoietic cell types in a patient with myelodysplastic syndrome (MDS)." (Ans. 3.)

The Examiner further finds that other steps in the claims, including "[u]sing antibodies to detect the marker profile of the cell types" and "[d]etermining the presence of a specific level of change in relation to a control value," do not amount to "significantly more than the law of nature." (*Id.* at 4)

Citing to the March 2014 Guidance,[3] Appellants contend that the claims recite something significantly different than a law of nature.

[3] U.S. Patent & Trademark Office, Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural

Appellants do not separately argue claims 6 and 7. We therefore limit our analysis to claim 1. The issue with respect to this rejection is whether the evidence of record support the Examiner's conclusion that the claims are directed towards non-statutory subject matter.

Principles of Law

> *In Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. [66] . . . (2012), the Supreme Court set forth a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. First, we determine whether the claims at issue are directed to a patent-ineligible concept. *Id.* at 1297. If the answer is yes, then we next consider the elements of each claim both individually and "as an ordered combination" to determine whether additional elements "transform the nature of the claim" into a patent-eligible application. *Id.* at 1298. The Supreme Court has described the second step of this analysis as a search for an "inventive concept"—i.e., an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Id.* at 1294.

Ariosa Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1371, 1375 (Fed. Cir. 2015).

Analysis

We analyze this case under the framework set forth by the Supreme Court in *Mayo* and applied by our reviewing court in *Ariosa*. With respect to the first step, whether claim 1 is directed to a patent-ineligible concept, we agree with the Examiner that claim 1 recites a patent-ineligible law of

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Phenomena, & Natural Products (March 4, 2014), available at https://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf.

nature, specifically, the relationship between hematopoietic stem and progenitor cell phenotype distribution and a diagnosis of MDS. (Ans. 3.) In *Mayo*, for instance, the Supreme Court found that a claim was directed to a natural law, where the claim required administering a drug and determining the levels of a metabolite following administration, wherein the level of metabolite was indicative of a need to increase or decrease the dosage of the drug. *See Mayo Collaborative Services v. Prometheus Labs., Inc.*, 566 U.S. 66, 74 (2012). Here, similarly, claim 1 states that "an increase in the fraction of HSC and a decrease in the fraction of myeloid progenitor cells that are granulocyte macrophage progenitor cells relative to a normal control of at least 1.5 fold is indicative of an initial diagnosis of myelodysplastic syndrome (MDS)."

Next, we consider whether claim 1 recites "an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Ariosa*, 788 F.3d at 1375 (citation omitted). We agree with the Examiner that it does not. (Ans. 4.) In particular, the Examiner found, and Appellants have not persuasively disputed, that "all of the antibodies used by the applicant for measuring hematopoietic stem or progenitor subsets in a hematological sample from the patient suspected of said myelodysplastic condition were known prior to the instant application" and that "these antibodies were used for measuring hematopoietic stem or progenitor subsets in hematological samples." (*Id.* at 10; *see also* Spec. ¶ 53 (stating that "[t]he details of the preparation of antibodies and their suitability for use as specific binding members are well-known to those skilled in the art"),

¶ 56 (stating that "[a] number of . . . methods are known in the art" for quantitating labeled cells as to the expression of cell surface markers).) Accordingly, we find that instant claim 1 is analogous to the claim found unpatentable in *Mayo.*

Appellants argue that the claims recite something significantly different than a law of nature based on the twelve factors enumerated in the March 2014 Guidance. As an initial matter, we note that the March 2014 Guidance is not law and also does not reflect the USPTO's current analysis protocols on subject matter eligibility. *See, e.g.*, 2014 Interim Guidance on Patent Subject Matter Eligibility, 79 Fed. Reg. 74618 (Dec. 16, 2014) ("2014 Interim Guidance); July 2015 Update on Subject Matter Eligibility, 80 Fed. Reg. 45429 (July 30, 2015) ("2015 Update"); May 2016 Subject Matter Eligibility Update, 81 Fed. Reg. 27381 (May 6, 2016) ("2016 Update") (collectively "Interim Guidance").

Neither are we persuaded by Appellants' arguments. Appellants first contend that the claims recite something significantly different than a law of nature because the claims do not preclude others from applying the natural principle, i.e., the correlation between progenitor cell distribution and MDS, in other methods. (Br. 3, 5.) However, "[w]hile preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility." *Ariosa*, 788 F.3d at 1379. Instead, as our reviewing court has explained, "[w]here a patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework, . . . , preemption concerns are fully addressed and made moot." *Id.* Here, as in *Ariosa*, Appellants' "attempt to limit the breadth of the claims by showing alternative uses of [the natural phenomenon] outside of the scope of the

claims does not change the conclusion that the claims are directed to patent ineligible subject matter." *Id.* Accordingly, even though the claims are limited to the use of antibodies to determine the distribution of progenitor cells and do not fully preempt the natural correlation, the claims remain ineligible because they are drawn to patent ineligible subject matter. *Id.*; *see also Ariosa*, 788 F.3d at 1377 (holding dependent claim invalid as lacking subject matter even though claim is limited to using a specific technique (polymerase chain reaction, or PCR) to amplify a particular type of DNA).

Appellants next argue that the claims are distinguishable from those in *Mayo* because the instant claims recite additional elements that relate to the natural principle in a significant way, e.g., diagnosing MDS using hematopoietic cell type distribution and providing the assessment to an individual, and further argue that

> the claimed elements do more than describe the natural principle with general instructions to apply it [because] the claim . . . recites an application . . . that is limited to measurement of expression levels of specific cell surface markers with specific antibodies, requires determining the presence of a specific level of change in relation to a control value, and providing a diagnosis.

(Br. 3–4, 5–6.) In particular, Appellants argue that "unlike the claims in *Mayo*, the asserted natural principle is required to be used," that "it is clear how the correlation is applied and used in order to determine a diagnosis," and that "determining a diagnosis is clearly an important and practical application of the alleged natural correlation." (*Id.*)

We are not convinced because, as in *Mayo*, the wherein clause of claim 1 "simply tell[s] a doctor about the relevant natural law[], at most adding a suggestion that he should take th[e] law[] into account when

treating his patient. That is to say, th[e] clause[] tell[s] the relevant audience about the law[] while trusting them to use th[e] law[] appropriately." *Mayo*, 566 U.S. at 78. Likewise, to the extent that claim 1 is an "important and practical application of the . . . natural correlation" between progenitor cell distribution and MDS diagnosis (Br. 4), the claim in *Mayo* was a similarly important and practical application of the natural correlation between the level of a particular metabolite in the blood and the appropriate dosage of a drug, 6-thioguanine, to be given to a patient. Nevertheless, the Supreme Court found that such application was insufficient for patentable utility because the claim "steps are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities." *Id.* at 80.

Finally, as we have already discussed, limiting the claim by requiring conventional steps such as "measur[ing] expression levels of specific cell surface markers with specific antibodies" and "determining the presence of a specific level of change in relation to a control value" do not suffice to render the claim patentable where such steps are merely conventional steps employed in the art. *Ariosa*, 788 F.3d at 1377 (explaining that "'[s]imply appending conventional steps, specified at a high level of generality,' [is] not enough to supply an inventive concept") (citing *Mayo*, 566 U.S. at 82).

We also note but are not persuaded by Appellants' argument that assaying for subsets of hematopoietic cells as recited in the claims requires "transformation" of a property of a biological molecule (i.e., concentration) into a detectable signal. (Br. 4.) Again, such "transformation" does not render a claim patentable where the method of detection is conventional: *Mayo* similarly involved a step of determining the concentration of a metabolite in the blood. *Mayo*, 566 U.S. at 74.

Finally, Appellants contend that claim 1 "recites steps that are more than well-understood, purely conventional or routine in the art," because "[i]t is not routine or conventional in the art to measure hematopoietic stem or progenitor subset distributions in a hematologic sample from a patient suspected of said myelodysplastic condition." (Br. 4, 5.) Again, we are not convinced. As the Examiner finds and the Specification acknowledges, antibody preparation and quantification of cells based on cell surface markers are known in the art. (Ans. 10; Spec. ¶¶ 53, 56.) That these conventional processes were not previously used to diagnose a patient with MDS does not distinguish the claims because "appending routine, conventional steps to a natural phenomenon, specified at a high level of generality, is not enough to supply an inventive concept." *Ariosa*, 788 F.3d at 1378. In *Ariosa*, for instance, claims relating to a method for detecting paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample were found to be directed to non-patentable subject matter even though, prior to the patent at issue, "*no one* was using the plasma or serum of pregnant mothers to amplify and detect paternally-inherited cffDNA [(cell-free fetal DNA)]." *Id.* at 1379; *see also id.* at 1381 (Linn, J., concurring).[4]

[4] We note that "a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made." *Mayo*, 566 U.S. at 79 (quotation marks and citation omitted). In this case, however, considering the additional steps of claim 1 as an ordered combination "adds nothing to the laws of nature that is not already present when the steps are considered separately," because anyone who wants to make use of the correlation between progenitor cell distribution and MDS diagnosis must first measure hematopoietic stem or progenitor subset distributions in a hematologic sample from a patient. *Id.* ("Anyone who wants to make use of [the

Accordingly, we affirm the Examiner's rejection of claim 1. Claims 6 and 7, which were not separately argued, fall with claim 1. 37 C.F.R. § 41.37(c)(1)(iv).

SUMMARY

For the reasons above, we affirm the Examiner's rejection of claims 1, 6, and 7.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

relationship between metabolite concentration and thiopurine drug] must first administer a thiopurine drug and measure the resulting metabolite concentrations, and so the combination amounts to nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients.").